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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,296	06/28/2004	Yuji Yamazaki	081356-0218	7715

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EXAMINER	
SKELDING, ZACHARY S	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
12/29/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,296	YAMAZAKI ET AL.	
	Examiner	Art Unit	
	ZACHARY SKELDING	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6 and 20-25* is/are pending in the application.

4a) Of the above claim(s) *1,2,4 and 6* is/are withdrawn from consideration.

5)☒ Claim(s) *20-22* is/are allowed.

6)☒ Claim(s) *23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11-18-09 10-27-09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's argument and amendments filed October 9, 2009 are acknowledged.

   Claims 1, 2, 4, 6 and 20-25 are pending.

   Claims 1, 2, 4 and 6 have been withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being directed to a non-elected Species.

   Claims 20-25 are under examination.

   This Office Action is in response to applicant's amendment and remarks filed October 9, 2009.

   The prior rejections of record can be found in the Office Action mailed April 10, 2009.

   The prior rejection under 35 U.S.C. § 102(b) has been withdrawn upon further consideration in view of applicant's argument.

   New Grounds of Rejection are put forth below.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

   > A person shall be entitled to a patent unless –
   >
   > (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claim 23 is rejected under 35 U.S.C. § 102(e) as anticipated by Econs et al. (WO 02/08271, cited on an IDS).

   Econs teaches the production of polyclonal anti-FGF23 antibodies capable of inhibiting the biological activity of FGF23 to treat diseases associated with hypophosphatemia, such as X-linked hypophosphatemic rickets. (see, e.g., page 6, last paragraph – p. 7, 1st paragraph; p. 23, 3rd paragraph; p 25, 2nd – p. 27, last paragraph).

Given that polyclonal antibodies bind throughout the length of the immunizing protein, the polyclonal antibodies of Econs would inherently compete with the claimed antibodies.

Since the Office does not have a laboratory to test the reference antibodies and determine if they compete with the instantly claimed antibodies, it is applicant's burden to show that the reference antibodies are not competitive with the instantly claimed antibodies. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald* et al., 205 USPQ 594 (CCPA 1980).

Applicant is reminded that as stated in MPEP § 2112.01, "[w]here the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada,* 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)."

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Econs et al. (WO 02/08271) in view of Ornitz et al. (Genome Biol. 2001;2(3): REVIEWS3005. Epub 2001 Mar 9), the ADHR consortium (Nat Genet. 2000 Nov;26(3):345-8), and Bowe (Biochem Biophys Res Commun. 2001 Jun 22;284(4):977-81), each of which was cited on an IDS.

Econs teaches the production of monoclonal and polyclonal anti-FGF23 antibodies capable of inhibiting the biological activity of FGF23 to treat diseases associated with hypophosphatemia, such as X-linked hypophosphatemic rickets. (see, e.g., page 6, last paragraph – p. 7, 1st paragraph; p. 23, 3rd paragraph; p 25, 2nd – p. 27, last paragraph). Econs

further teaches that either in vivo or in vitro assays can be used to test for FGF23 hypophosphatemic activity and that one use of either assay is to identify inhibitors of FGF23 activity such as anti-FGF23 antibodies (see page 22, 2nd paragraph; p. 24, 1st paragraph; p. 25, 1st paragraph; page 29, 3rd paragraph through page 30, 1st paragraph). For example, Econs teaches the ability of FGF23 to induce hypophosphatemia in vitro can be assessed by measuring the effect of FGF23 on phosphate transport in isolated renal tubules or cell culture models possessing the necessary FGF23 signal transduction machinery (see ibid), and example of the later being provided by the teachings of Bowe at page 979, right column, 1st paragraph. Likewise, Econs teaches the ability of FGF23 to induce hypophosphatemia in vivo can be analyzed, e.g., by making mice transgenic for FGF-23 or by injecting purified FGF-23 (see Example 4 on pages 76-77).

Given the teachings of Econs one of ordinary skill in the art would have been motivated to prepare an anti-FGF23 antibody that is capable of inhibiting the hypophosphatemic activity of FGF23 because such an antibody would be useful in treating hypophosphatemic diseases such as X-linked hypophosphatemic rickets.

However, Econs differs from the claimed invention in that it does not explicitly direct one of ordinary skill in the art to make monoclonal antibodies that compete with the claimed antibodies and it does not explicitly teach pharmaceutical compositions of antibodies that compete with the claimed antibodies.

Nevertheless, it would have been immediately obvious to one of ordinary skill in the art that antibodies, i.e., proteins naturally found in the blood stream, designed to inhibit a blood-borne protein such as FGF-23 need to be present in a pharmaceutically acceptable carrier so that they can be administered by injection into the blood stream.

Moroever, in considering how to make such antibodies one of ordinary skill in the art would have known that while the extended C-terminal portion of FGF-23 distinguishes it from the other FGFs known in the art (see, e.g., the ADHR consortium Figure 3 legend), and that this region is most likely involved in FGF23 activity because mutations that inhibits FGF23 proteolytic degradation increase its hypophosphatemic activity (see, e.g., Econs at page 28, 1st paragraph and the paragraph bridging pages 74-75), the N-terminal portion of FGF23 extending upstream from the FGF-23 unique C-terminus would have been considered by one of ordinary skill in the art to have been an even better target for an anti-FGF23 antibody. This is because the N-terminal region of FGF-23 was known to correspond to the FGF family β strand core which contains the residues known in the art to mediate the interaction of FGF family members with the FGF receptors as well as with heparin (see Ornitz at page 2, right column, last paragraph, and Figure 3), and furthermore FGF-23, like the other members of the FGF family was known to interact with the FGF receptors and heparin (see, e.g., Econs at page 76, 1st paragraph and the paragraph bridging pages 24-25). Thus, in view of the prior art teachings it would have been obvious to one of ordinary skill in the art, and one of ordinary skill in the art would have been motivated and would have had a reasonable expectation of successfully preparing anti-FGF23 antibodies capable of inhibiting

the hypophosphatemic activity of FGF23 using the N-terminal "core" domain portion of FGF-23.

Since the Office does not have a laboratory to test the reference antibodies and determine if they compete with the instantly claimed antibodies, it is applicant's burden to show that the reference antibodies are not competitive with the instantly claimed antibodies. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald* et al., 205 USPQ 594 (CCPA 1980).

Applicant is reminded that as stated in MPEP § 2112.01, "[w]here the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada,* 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)."

6. Claims 20-22 are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY SKELDING whose telephone number is (571)272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

   If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

   Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachary Skelding/
Examiner, Art Unit 1644